FACT SHEET
Healthcare Provider

Homocystinuria

Description:
Homocystinuria (HCU) is an autosomal recessive disorder caused by a defect in the catabolism of sulfur-containing amino acids. The most common cause of HCU is a deficiency of the enzyme cystathionine B-synthase. Elevated levels of hymocysteine, methionine, and metabolites of homocysteine accumulate in the blood and urine of these patients.

Incidence in General Population:
1: 150,000 live births

Symptoms:
Typically the child with HCU is asymptomatic in the first few months of life.

Untreated Clinical Features

- Physical Disabilities: Marfanoid habitus, ectopia lentis, glaucoma, cataracts, osteoporosis with bone deformities, high palatal arch, and muscle weakness with a shuffling gait.
- Developmental Disabilities: Mental retardation, developmental delay is reported in 65% to 80% of untreated individuals.
- Mortality: Frequently due to thromboembolism in cerebral, pulmonary, renal, and myocardial circulation. Death usually occurs within the first year of life. Death can also occur later from thromboembolism.

Symptomatic Diagnosis

A symptomatic diagnosis is limited due to nonspecific features during the newborn period. Ocular abnormalities, because of their distinctive lens displacement, may be the only symptoms leading to an early clinical diagnosis.

Variants:

There are several forms of HCU that are characterized by normal or low blood levels of methionine and the absence of ocular abnormalities. These variants are additional disorders of methionine metabolism, including decreased N5 methyltetrahydrofolate homocysteine methyltransferase activity due to vitamin B12 deficiency and decreased N5, 10-methyl tetrahydrofolate reductase activity.

Diagnosis:
Newborn Screening—Tandem mass spectrometry identifies elevations in blood methionine on dried-blood-spot filter paper. A normal range is 0-61 μmol/l. A second dried-blood-spot filter paper card may be requested by the Newborn Screening Laboratory if the initial screening result is above the normal range. Infants with presumptive positive screening (critical) results require prompt follow up. If this occurred, the clinician would be contacted by the Metabolic Treatment Center. When notified of these results, the clinician should immediately check on the clinical status of the baby and facilitate referral to the Metabolic Treatment Center. The Metabolic Treatment Center will provide consultation and assistance with diagnostic testing.

Monitoring:
Individuals diagnosed with HCU require life-long medical management and dietary therapy coordinated by nutrition and metabolic specialists. Clinical observation is important for healthcare providers caring for patients with Biotinidase. It is important for primary care provider and the Metabolic Center to develop an ongoing collaborative relationship in caring for these patients.

Treatment:
Early diagnosis and treatment is essential for an improved prognosis. Children identified during the newborn period, or even later in infancy, can prevent or greatly reduce the severity of the clinical consequences. Individuals with HCU require a diet restricted in methionine and supplemented with cystine and medication (betaine). Folic acid and B12 supplements may be beneficial for some patients. Anticoagulants may also be indicated but not typically for infants. Some individuals with HCU may respond to vitamin B6 (pyridoxine) supplements.

Illness and Immunizations:
- Immunizations should be kept current.
- Consult with the Metabolic Treatment Center within 24 hours of the onset of an illness or at the time of hospitalization.

Growth and Development:
Monitor the child for normal growth and development.

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